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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,998	01/04/2001	Ernst H. Rinderknecht	P0941C1D1C1	4682

9157 7590 10/30/2002

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 10/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/754,998	RINDERKNECHT ET AL	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-29* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of the species A **without** traverse of an antibody that binds p185 HER2 in Paper No. 11 is acknowledged. Claims 19-28 will be examined to the extent they read on the elected species. Because the response was made without traverse the restriction/election is deemed proper and made **Final**.

2. Claim 29 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

3. Claims 19-28 are under examination. The claims are being examined to the extent the species is an antibody to P185 HER2.

Specification

4. The disclosure is objected to because of the following informalities:

a. Page 2, line 17 contains an incomplete citation as it lacks the volume number. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 19-26 are indefinite for reciting "an antibody prepared....eluting the antibody from the column with a buffer having a pH of about 2.5-4.5, and (b) a physiologically acceptable carrier" in claim 19 because the exact meaning of the phrase is unclear. It is unclear how the antibody can be in a buffer of 2.5-4.5 and be in a physiological acceptable carrier when physiological pH is 7. Is the antibody at pH 2.5-4.5 or at pH 7?. In addition it appears the process is missing an essential step from where the antibody is at pH2.5-4.5 to physiological pH.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 19-20, 23-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-10 of U.S. Patent No. 6,066,719. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims in the instant application are drawn to compositions comprising an antibody linear F(ab')2 fragment and a physiologically acceptable carrier wherein the antibody binds p185 HER2 and the fragment is greater than 98% purity. The claims in the patent recite a linear VH-CH1-VH-CH1 heavy chain and two light chains which binds p185 HER2 and compositions comprising such. Since the linear VH-CH1-VH-CH1 associated with two light chains is the same as a linear F(ab')2 fragment and both bind p185 HER2 the fragments are the same in the instant claims and the patent. Since the patent claims are to the linear antibody fragment, it would be obvious that the product in the patent is greater than 98% purity and as such it would be obvious to combine the pure product in a composition comprising a pharmaceutically acceptable carrier.

Claims 19-20, 23-28 are directed to an invention not patentably distinct from claims 1, 3-10 of commonly assigned 6,066,719. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 6,066,719, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the

examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 19-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Carter et al (U.S. Patent 6,054,297, filed 5/95 and is a CON filed 8/92).

The claims recite a composition comprising an antibody prepared by a process and a physiologically acceptable carrier wherein the antibody is a correctly disulfide linked antibody and a F(ab')2. Further claimed is wherein the antibody is a humanized antibody or humanized antibody fragment and wherein the antibody binds P185 HER2.

Carter et al teach a humanized antibody to P185 HER2 wherein the antibody can be a F(ab')2 fragment (see column 8, lines 65-67) and the antibody can be in a physiologically acceptable carrier (see column 46, lines 16-45).

Claim 19 recites a composition comprising an antibody produced by a process. The method in which the antibodies were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

11. Claims 19, 21, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Hudziak et al (WO 89/06692, published 7/89).

The claims have been described supra.

Hudziak et al teach an antibody that binds P185 HER2 and the antibody can be a humanized antibody (see page 8, lines 3 and 17 and page 17, lines 3-11) and compositions comprising pharmaceutically acceptable carriers (see page 21, lines 18-29).

Claim 19 recites a composition comprising an antibody produced by a process. The method in which the antibodies were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 19-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter et al (U. S. Patent 6,054,297, filed 5/95 with priority as a CON to 8/92) as applied to claims 19-25 above, and further in view of Morimoto et al (J. Biochem. Biophys. Methods 24:107-17, 1992, IDS #4.5).

Claims 19-25 have been described supra. Claims 26-28 recite wherein the purity of the antibody fragment is greater than 98% and wherein the antibody binds P185 HER2.

Carter et al has been described supra. Carter et al does not specifically teach the purity of the antibody fragment is more than 98% pure. This deficiency is made up for in the teachings of Morimoto et al .

Morimoto et al teach a F(ab')2 fragment of an antibody that is purified to greater than 98% and the antibody fragment was eluted with PBS (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the method of Morimoto et al with the antibody of Carter et al to purify the antibody fragment to greater than 98% purity.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the method of Morimoto et al with the antibody of Carter et al to purify the antibody fragment to greater than 98% purity because Morimoto et al teach a single step purification of five antibodies that were fragmented and purified to greater than 98% purity (see entire document, especially page 108, 112). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the method of Morimoto et al with the antibody of Carter et al to purify the antibody fragment to greater than 98% purity because Carter et al teach fragments of the antibody and it would have been obvious to obtain the purest preparation and to use an efficient method as described by Morimoto et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

14. Claim19-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hudziak et al (WO 89/06692, published 7/89) as applied to claim19, 21, 23 above, and

further in view of Morimoto et al (J. Biochem. Biophys. Methods 24:107-17, 1992, IDS #4.5).

The claims have been described supra.

Hudziak et la has been described supra. Hudziak et al does not teach antibody fragments or humanized antibody fragments or purified fragments that are greater than 98% purity. This deficiency is made up for in the teachings of Morimoto et al .

Morimoto et al has been described supra. Morimoto et al also teach F(ab')2 are currently of great interest for both diagnostic and therapeutic agents because they do not retain any biological functions due to Fc regions and interaction with non-specific proteins is reduced (see page 108).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the method of Morimoto et al with the antibody of Carter et al to purify the antibody fragment to greater than 98% purity.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the method of Morimoto et al with the antibody of Hudziak et al to purify the antibody fragment to greater than 98% purity because Morimoto et al teach a single step purification of five antibodies that were fragmented and purified to greater than 98% purity (see entire document, especially page 108, 112). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the method of Morimoto et al with the antibody of Hudziak et al to purify the antibody fragment to greater than 98% purity because Hudziak et al teach the antibodies can be used for imaging and

therapy and as taught by Morimoto et al F(ab')2 fragments are better for these studies and therapies.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the

Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879